

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Jorg Stürzebecher et al.	Confirmation No.:	1588
Serial No.:	10/506,579	Art Unit:	1621
Filed:	April 13, 2005	Examiner:	P. Zucker
Customer No.:	21559		
Title:	UROKINASE INHIBITORS, PRODUCTION AND USE THEREOF		

Commissioner for Patents  
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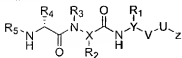
DECLARATION OF ANDREA SCHWEINITZ UNDER 37 C.F.R. § 1.132

TRAVERSING GROUNDS OF REJECTION

Under 37 C.F.R. § 1.132 and regarding the rejection of claims 21 and 34-38 in view of Levy et al., WO 02/14349 ("Levy"), I declare:

1. I am an inventor of the subject matter that is described and claimed in the above-captioned patent application.
2. As recited in currently amended claim 21, at least one of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> or R<sub>5</sub> includes one or more radicals, selected from -COOH, -CH(COOH)<sub>2</sub>, -SO<sub>2</sub>H, NH<sub>2</sub>, an amidino, hydroxyamidino, amidrazono, or guanidino group, or a salt of any of these groups. The Office has cited the compound described in Example 45 of Levy, benzylsulfonyl-D-serine-L-alanine-3-guanidinobenzylamide ("the Levy compound"). As shown in the following table, the Levy -CH<sub>2</sub>OH corresponds to R<sub>4</sub> in formula I and the Levy compound does not include any groups that satisfy the claimed structural requirements for any of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, or R<sub>5</sub> in instant formula I.

**Corresponding Groups in Instant Formula I:**



$R_1 = H$ ;

$R_2 = CH_3$ ;

$R_3 = H$ ;

$R_4 = -(CH_2)_fOR_{11}$ , where  $f=1$  and  $R_{11}$  is H;

$R_5 = -SO_2R_{12}$ , where  $R_{12}$  = unsubstituted aralkyl;

$U$  = phenyl;

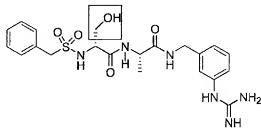
$V = (CH_2)_n$ , where  $n = 0$ ;

$X = CH$ ;

$Y = (CH)_m$ , where  $m = 1$ ; and

$Z$  = occurs in the 3-position and is a guanidino group

**The Levy Compound:**



In this structure,  $R_1$  and  $R_3$  are each H,  $R_2$  is  $CH_3$ , and  $R_5$  is  $SO_2CH_2Ph$ , and none of these groups includes a radical selected from  $-COOH$ ,  $-CH(COOH)_2$ ,  $-SO_2H$ ,  $NH_2$ , an amidino, hydroxyamidino, amidrazono, or guanidino group, or a salt thereof. The Levy compound is therefore not encompassed by the claimed chemical genus.

3. Further, the 1:1  $CH_2Cl_2/CF_3CO_2H$  solution described in Levy Example 45 would not be sufficient to protonate the serine  $-CH_2OH$  group. The  $pK_a$  of a protonated serine  $-OH$  group is approximately -2.85 and the  $pK_a$  of  $CF_3CO_2H$  is approximately -0.2. Based on these  $pK_a$  differences, a chemist would not expect the serine  $-OH$  group of the Levy compound to be protonated in the  $CH_2Cl_2/CF_3CO_2H$  solution ( $pH \sim 1-2$ ), in the isolated compound obtained according to the procedure described in Levy Example 45, or in the stomach ( $pH \sim 1-1.5$ ). Consequently, a chemist would recognize that the Levy  $-CH_2OH$  group is neutral under these conditions and that none of the  $R_1$ ,  $R_2$ ,  $R_3$ , or  $R_5$  groups in the Levy compound includes the structural features recited in the instant claims.

4. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

26.03.2010

Date

A. Schweinitz

Dr. Andrea Schweinitz